REMARKS

Reconsideration and allowance of the above application are respectfully requested. Claims 16-20 are pending in this application. By this Amendment, Applicants have amended the claims to refer to methods of treating a medical condition of the type that is characterized by the destruction of articular cartilage in a human subject by administering an aryl-alkoxy-aryl substituted hydroxamic acid compound to a human, wherein the carboxylic acid hydroxamide derivative exhibits an aggrecanase IC_{50} of less than about 20 nM, said aggrecanase IC_{50} measured by an aggrecanase chondrocyte assay. Support for this amendment to the claims can be found in the instant specification, inter alia, at page 5, lines 1-5. Thus, Applicants have not introduced new matter by these amendments. The foregoing amendments are being submitted in the interests of advancing prosecution on the merits and do not constitute a representation or concession as to the propriety of the rejections of record.

Rejection Under 35 U.S.C. ¶ 112, First Paragraph

Claims 16-20 were rejected under 35 U.S.C. ¶ 112, first paragraph, for failing to comply with the written description requirement. The claim(s) were alleged to contain subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the art that the inventor(s) had possession of the claimed invention at the time the application was filed. The claims were also rejection under 35 U.S.C. ¶ 112, first paragraph, for failing to comply with the enablement requirement. The Examiner asserted that the specification does not reasonably provide enablement for making all the carboxylic acid hydroxamides with the desired aggrecanase activity they intend to use.

Without conceding the propriety of the rejection, Applicants have amended the claims to refer to hydroxamide compounds bearing an aryl-alkoxy-aryl substituent. Thus, by this amendment, Applicants have added one more layer of detail to the description of the compounds falling within the scope of the claims: to wit, not only are they hydroxamide derivatives, but they are hydroxamide derivatives bearing an aryl-alkoxy-aryl substituent. Moreover, the claims further define the class of compounds that fall within the claims by adding a significant functional limitation on the compounds: they must exhibit an aggrecanase IC_{50} of less than about 20 nM, said aggrecanase IC_{50} measured by an aggrecanase chondrocyte assay. Therefore, Applicants have identified the compounds that fall within the scope of the instant claims by virtue of several structural, as well as functional limitations, which fully complies with the legal standards for written description noted by the Examiner in the Official Action, e.g., Lockwood, Pfaff, Amgen, and Enzo Biochem.

Moreover, as to the enablement rejection, the Examiner alleges that because "Applicants do not specify the structures of the compounds they intend to use, how can the skilled process chemist be expected to make these compounds?" 6-10-03 Official Action at 4.

First, contrary to the Official Action, the claims are not directed to any compound having the claimed selectivity: they are expressly and unequivocally directed to a hydroxamic acid compound bearing an aryl-alkoxy-aryl substituent. The reader thus knows exactly which class of compounds to consider. Moreover, the reader is given examples (non-limiting) of such compounds, both in the guise of a Formula I genus, and then from the various specific embodiments. This guidance is directive as to hyroxamic acids suitable for the present invention. That not every possible hydroxamic acid manifesting the requisite behavior may be encyclopedically delineated *pro arguendo* is of no moment inasmuch as an Applicant is not required to so exhaustively and definitively list. Indeed, the Official Action concedes enablement for certain compounds, but takes the position that any need on the reader's part to undertake some effort to identify compounds (again: hydroxamic acids) beyond this forecloses enablement.

This is not the case in fact or law: factually, the specification provides clear cut directions on the type of compounds and assays to be used for the claimed method of treatment: hydroxamic acid compounds bearing an aryl-alkoxy-aryl substituent, exhibiting an aggrecanase IC_{50} of less than about 20 nM, said aggrecanase IC_{50} measured by an aggrecanase chondrocyte assay. The specification provides general and specific examples of compounds falling within the scope of this claim and how to identify other members of the class. That is simply all that is required.

Legally, making and testing (experimentation) is quite permissible under 112. Indeed, a sizeable amount of experimentation is perfectly acceptable, if routine. The prohibition is not to the amount of experimentation, but to the burden of it: if it veers from the ordinary to the extraordinary then and only then are 112, 1st ¶ issues raised. See e.g. PPG Indus. Inc. v. Guardian Indus. Corp. 37 USPQ2d 1618, 1623 (Fed Cir 1996):

> "The test is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed...."

In this regard, Applicants take issue with the Examiner's description of the skilled artisan (see page 5 of the June 10, 2003 Official Action). The Examiner characterizes the skilled artisan as a process chemist or pilot plant operator with a BS degree in chemistry and several years of experience. One must also add that the skilled artisan is familiar with the field of the application. In this regard, the Examiner's attention is directed to MPEP §2164.05(b), and Technicon Instruments Corp. V. Alpkem Corp., 664 F. Supp 1558, 1580 (US Dist., 1986). In Technicon, the court found that in order to comply with section 112

> the description must be sufficient to allow someone with ordinary skill in the art to which it pertains or with which it is most clearly connected to practice the invention. The specification needs to describe the invention only in such detail as to enable a person

> skilled in the most relevant art to make and use it. When an invention, in its different aspects, involves distinct arts, the specification is adequate when it enables those who have the best chance of being able to carry out the aspect related to their specialty. If two distinct technologies are relevant to an invention, then the disclosure will be adequate if a person of ordinary skill in each of the two technologies could practice the invention from the disclosures. The person of ordinary skill in the field must be someone who is skilled in the design of the devices in question, not just in the use of the device.

(Citations omitted and emphasis added.)

In Technicon, the court held that the skilled artisan was a scientist that was particularly familiar with the specific field that was the foundation of the claims. Therefore, in view of the foregoing, Applicants submit that the skilled artisan who would be interpreting the claims of the present application and putting them into practice would be a skilled organic chemist, familiar with the state of the art in aggrecanase inhibitors, and particularly, hydroxamide aggrecanase inhibitors. Therefore, we can attribute to that skilled artisan, a significant familiarity with the claimed class of compounds, which includes their synthesis and how other hydroxamide compounds interact with and thereby inhibit aggrecanase. Thus, the skilled artisan is not a relative novice, but something of an expert in the field. As such, he or she would undoubtedly find the instant specification more than enables the full scope of the claims and to provide more detail than what is already provided would be superfluous.

Thus, in view of the foregoing amendments and arguments, Applicants submit that the Section 112, rejections are untenable and should be withdrawn.

Rejection Under 35 U.S.C. §102(e)

The claims were also rejected under 35 U.S.C. § 102(e) as anticipated by Robinson ('361 patent), Reiter ('392 patent), Duan ('336 patent), or Bender ('653 patent). With respect to each of these references, the Examiner concedes that the reference is silent as to the potencies of aggrecanase enzyme inhibition of the disclosed compounds and that "for all the Examiner knows, the compounds taught in [Robinson, Reiter, Duan, or Bender] do have the required potency." Official Action at 7-10.

To anticipate a claim, a single source must contain all of the elements of the claim. See Hybritech Inc. v. Monoclonal Antibodies, Inc., 802 F.2d 1367, 1379, 231 U.S.P.Q. 81, 90 (Fed. Cir. 1986); Atlas Powder Co. v. E.I. du Pont De Nemours & Co., 750 F.2d 1569, 1574, 224 U.S.P.Q. 409, 411 (Fed. Cir. 1984); In re Marshall, 578 F.2d 301, 304, 198 U.S.P.Q. 344, 346 (C.C.P.A. 1978). The prior art need not expressly disclose a newly identified aspect of a claimed invention to anticipate it, but "may anticipate by inherency where it would be appreciated by one of ordinary skill in the art." Glaxo Inc. V. Novopharm Ltd., 52 F.3d 1043, 1047 (Fed. Cir. 1995).

Applicants respectfully direct the Examiner's attention to the Federal Circuit's explanation of the standard that should be used to determine inherency:

> To serve as an anticipation when the reference is silent about the asserted inherent characteristic, such gap in the reference may be filled with recourse to extrinsic evidence. Such evidence must make clear that the missing descriptive matter is necessarily present in the thing described in the reference.
>
> Inherency . . . may not be established by probabilities or possibilities. The mere fact that a certain thing may result from a given set of circumstances is not sufficient. If, however, the disclosure is sufficient to show that the natural result flowing from the operation as taught would result in the performance of the questioned function, it seems to be well settled that the disclosure should be regarded as sufficient.

Continental Can, 948 F.2d at 1268-69 (emphasis added).

It is also noteworthy that the Board of Appeals has also weighed in on this issue and the Board has provided the following guidelines for examining applications in this context: "[t]o support an anticipation rejection based on inherency, an examiner must provide factual and technical grounds establishing that the inherent feature necessarily flows from the teachings of the prior art." See Ex parte Levy, 17 USPQ 2d 1461, 1464 (BPAI 1990); see also In re Oelrich, 666 F.2d 578, 581 (CCPA 1981), (holding that inherency must flow as a necessary conclusion from the prior art, not simply a possible one).

Applicants submit that the Examiner's arguments are simply deficient as a matter of law. In order to establish that the prior art compounds exhibit the biological activity described and claimed in the instant application, the law clearly establishes that the Examiner must point to some evidence in either the prior art references themselves or some other extrinsic evidence that would show that those prior art compounds necessarily exhibit the biological activity claimed in every instance. See also Glaxo Inc. v. Novopharm Ltd, 52 F.3d 1043, 1047 (Fed. Cir. 1995) (finding no inherent anticipation where the practice of the prior art method could yield crystals of either form, rather than always yielding a specific crystalline form). The Examiner's conclusion that "for all the Examiner knows, the compounds taught in [Robinson, Reiter, Duan, or Bender] do have the required potency" simply isn't good enough. The Examiner bears the burden of establishing a prima facie case of inherency according to the standards outlined above, and he simply has not met that burden as a matter of law. Accordingly, reconsideration and withdrawal of the Section 102(e) rejections are requested.

In view of the foregoing amendments, Applicants submit that the claims are in condition for allowance and such action is earnestly solicited.

Respectfully submitted,

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Pfizer Inc.
Patent Dept., 5th Fl.
150 East 42nd Street
New York, NY 10017-5755
(212) 733-6031

Pamela C. Ancona, Ph.D.
Attorney for Applicants
Reg. No. 41,494